PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K 14/555, A61K 9/14, 38/21 — A1

(11) International Publication Number: WO 95/31479

(43) International Publication Date: 23 November 1995 (23.11.95)

(21) International Application Number: PCT/US95/06008

(22) International Filing Date: 15 May 1995 (15.05.95)

(30) Priority Data:
08/246,034 18 May 1994 (18.05.94) US

(60) Parent Application or Grant
(63) Related by Continuation
US 08/246,034 (CIP)
Filed on 18 May 1994 (18.05.94)

(71) Applicant (*for all designated States except US*): INHALE THERAPEUTIC SYSTEMS, INC. [US/US]; 1001 East Meadow Circle, Palo Alto, CA 94303 (US).

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): PLATZ, Robert, M. [US/US]; 324 Valdez Avenue, Half Moon Bay, CA 94019 (US). KIMURA, Narinobu [JP/JP]; Basic Research Laboratories, Toray Industries, Inc., 1111 banchi, Tehiro, Kamakura-shi, Kanagawa-ken (JP). SATOH, Oichiro [JP/JP]; Basic Research Laboratories, Toray Industries, Inc., 1111 banchi, Tehiro, Kamakura-shi, Kanagawa-ken (JP). FOSTER, Linda, C. [US/US]; 733 Carolina Avenue, Sunnyvale, CA 94086 (US).

(74) Agents: MORAN, Tom, M. et al.; Cooley Godward Castro Huddleson & Tatum, Five Palo Alto Square, 3000 El Camino Real, Palo Alto, CA 94306-2155 (US).

(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN. European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published
With international search report.

(54) Title: METHODS AND COMPOSITIONS FOR THE DRY POWDER FORMULATION OF INTERFERONS

(57) Abstract

According to the present invention, methods and compositions are provided for spray-dried, interferon-based dry powder compositions, particularly interferon-beta. The compositions are useful for treating conditions in humans that are responsive to treatment with interferons. In particular, the methods of the present invention rely on spray drying to produce stable, high-potency dry powder formulations of interferons, including but not limited to IFN-beta. Surprisingly, it has been found that IFN can be prepared in high potency, dry powder formulations by spray drying. Such dry powder formulations find particular utility in the pulmonary delivery of IFN.

THE SUBJECT MATTER CLAIMED IS:

1. A spray-dried, interferon-based dry powder composition for pulmonary delivery, said composition comprising a therapeutically effective amount of interferon in combination with a pharmaceutically acceptable carrier.

2. The composition of claim 1, wherein the composition is substantially free from penetration enhancers.

3. The composition of claim 2, wherein the carrier comprises human serum albumin.

4. The composition of claim 3, wherein the carrier further comprises a carbohydrate bulking agent.

5. The composition of claim 4, wherein the carrier is mannitol.

6. The composition of claim 4, wherein the carrier is raffinose.

7. The composition of claim 1, wherein about 95% of the mass of the dry powder composition has a particle size of less than 10 μm.

8. The composition of claim 7, wherein about 80% of the mass of the dry powder composition has a particle size of less than 5μm.

9. The composition of claim 1, wherein the interferon is naturally occurring.

10. The composition of claim 1, wherein the interferon is interferon beta.

11. A unit dosage form for pulmonary delivery of interferon, which dosage form comprises a unit dosage receptacle containing a spray-dried, interferon-based dry powder composition, which composition comprises a therapeutically effective amount of an interferon in combination with a pharmaceutically acceptable carrier.

12. The unit dosage form of Claim 11, wherein the carrier comprises human serum albumin or human serum albumin and a carbohydrate bulking agent, the composition is substantially free from penetration enhancers and about 95% of the mass of the dry powder composition has a particle size of less than about 10μm.

13. A method of treating a disease state responsive to treatment by interferon, which method comprises pulmonarily administering to a subject in need thereof a physiologically effective amount of a spray-dried, interferon-based dry powder composition that comprises a therapeutically effective amount of an interferon in combination with a pharmaceutically acceptable carrier.

14. The method of Claim 13, wherein the carrier comprises HSA and a carbohydrate bulking agent, the composition is substantially free from penetration enhancers and about 95% of the mass of the dry powder composition has a particle size of less than about 10μm.

15. A method for aerosolizing a spray-dried, interferon-based dry powder composition that comprises a therapeutically effective amount of an interferon in combination with a pharmaceutically acceptable carrier, which method comprises:

dispersing an amount of the dry powder composition in a gas stream to form an aerosol and

capturing the aerosol in a chamber suitable for subsequent inhalation by a patient.

16. The method of claim 15, wherein the carrier comprises HSA and a carbohydrate bulking agent, the composition is substantially free from penetration enhancers and about 95% of the mass of the dry powder composition has a particle size of less than about 10μm.

17. A method for preparing a spray-dried, interferon-based dry powder composition that comprises a therapeutically effective amount of an interferon and a pharmaceutically acceptable carrier, which method comprises spray-drying an aqueous mixture of the interferon and the carrier under conditions to provide a respirable dry powder.

18. The method of Claim 17 wherein the composition is substantially free from penetration enhancers.

19. The method of Claim 18, wherein the carrier comprises HSA.

20. The method of Claim 19, wherein the carrier further comprises a carbohydrate bulking agent.

21. The method of Claim 20, wherein the bulking agent is mannitol.

22. The method of Claim 20, wherein the bulking agent is raffinose.

23. The method of Claim 17, wherein 95% of the mass of the spray-dry composition has a particle size less than 10 μm.

24. A spray-dried, interferon-based dry powder composition for pulmonary delivery, said composition comprising a therapeutically effective amount of naturally occurring interferon-beta in combination with a pharmaceutically acceptable carrier that comprises human serum albumin or human serum albumin and a carbohydrate bulking agent, wherein the composition is substantially free from penetration enhancers and about 95% of the mass of the dry powder composition has a particle size of less than 10 μm.

25. The composition of Claim 24, wherein the bulking agent is mannitol.

26. The composition of Claim 24, wherein the bulking agent is raffinose.